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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
7826513/AJC/AJS/MXK		
International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/AU2003/000660	30 May 2003	31 May 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl.[7] C12M 1/42; C12N 5/12, 5/16, 5/28, 13/00; A61K 48/00, 35/54

Applicant

APOLLO LIFE SCIENCES PTY LIMITED et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of **10** sheet(s).

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [X] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of the report
17 December 2003	7 September 2004
Name and mailing address of the IPEA/AU	Authorized Officer
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/000660

I. Basis of the report

1. With regard to the elements of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages 1-43, as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [X] the claims, pages , as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages 44-53, received on 22 June 2004 with the letter of 22 June 2004
- [X] the drawings, pages 1-24, as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be nonobvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos: **48-50**

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim Nos. **48-50**

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	5-7, 10-13, 20, 22, 25-33, 35-47, 51-71	YES
	Claims	1-4, 8-9, 14-19, 21, 23-24, 34	NO
Inventive step (IS)	Claims	44, 51-71	YES
	Claims	1-43, 45-47	NO
Industrial applicability (IA)	Claims	1-71	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

D1 Scott-Taylor et al. (2000, identified in the ISR)

D2 Krivokharchenko et al. (2002, identified in the ISR)

D3 Iwasaki et al. (2000, identified in the ISR)

D4 US 5589047 A (Coster et al.) 31 December 1996 (identified in the ISR)

D5 EP 0338667 A1 (Preece and Follet) 25 October 1989 (identified in the ISR)

D6 WO 1989/003426 A2 (Baylor College of Medicine) 20 April 1989 (identified in the ISR)

D7 WO 1998/056893 A1 (Walters et al.) 17 December 1998 (identified in the ISR)

D8 WO 2001/009297 A1 (A+ Science Invest AB) 8 February 2001 (identified in the ISR)

D9 WO 2002/010346 A2 (University of Ulster) 7 February 2002 (identified in the ISR)

D10 WO 2002/032378 A2 (Ohno) 25 April 2002 (identified in the ISR)

NEW CITATION

D11. Vienken J, Zimmermann U, Fouchard M, Zagury D. Electrofusion of myeloma cells on the single cell level. Fusion under sterile conditions without proteolytic enzyme treatment. FEBS Lett. 1983;163(1):54-6.

Claims 1 and 18 have been amended to include the selection of at least one pair of cells, which are then individually positioned between electrodes prior to an electrofusion process. It is noted that claims 1 and 18 are limited to methods and apparatus wherein the selected cell or pair/s of cells do not contact either electrode.

Novelty (N) claims 1-4, 8-9, 14-19, 21, 23-24, 34.

D11 discloses a method of fusing at least one pair of cells that are individually positioned between two electrodes prior to the application of dielectrophoresis and a predetermined fusion pulse (see the whole document). D11 is considered to deprive claims 1-4, 8-9, 14-19, 21, 23-24, and 34 of novelty.

Claims 5-7, 10-13, 20, 22, 25-33, 35-47, 51-71 meet the criteria set forth in PCT Article 33(2) for novelty. The prior art published before the priority date does not disclose a second pair of electrodes, or an automated drive, cell selection or pipette system

Inventive step (IS) claims 1-43, 45-47.

Claims 1-4, 8-9, 14-19, 21, 23-24, and 34 are already lacking novelty over D11, and also lack an inventive step.

D1 provides a method of fusing cells by electrofusion (see the whole document, particularly the abstract and sections 2.2-3.7 starting on page 267). D1 is directed to bulk electrofusion. There is no teaching in D1 to individually position and fuse pairs of single cells.

Supplemental Box I
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

Inventive step (IS) claims 1-43, 45-47 (continued)

D2 provides a method of fusing rat embryos to produce tetraploid blastocysts by chemical and electrical means (see the whole document, particularly the abstract, and "fusion of two-cell rat embryos" on page 461). D2 does not disclose the fusion of individual cells, but rather the fusion of individually positioned two-cell embryos.

D3 provides a method of producing tetraploid embryos by electrofusion (see the whole document, particularly the abstract and "production of tetraploid embryos" on page 471). Furthermore, these embryos are shown to develop into viable chimeras following aggregation with embryonic stem cells and subsequent transfer to the womb. D3 does not disclose the fusion of individual cells, but rather the fusion of individually positioned two-cell embryos.

D5 provides an automated cell fusion apparatus suitable for producing hybridomas (see the whole document). D5 is directed to bulk electrofusion techniques.

D6 discloses apparatus and methods for fusing cells using radiofrequency electrical pulses (see the whole document, particularly page 5 line 23 - page 8 line 24, page 13 line 29 - page 15 line 5, and examples IV and V). D6 is directed to bulk electrofusion.

D7 provides methods and apparatus for electrofusion of cells. The apparatus has a plurality of paired electrodes, to which different electrical fields may be applied (see the whole document, particularly page 20 line 26 - page 32 line 30, and figures 9-13). D7 is directed to bulk electrofusion.

D9 provides methods and apparatus for electrofusion of insulin producing cells (see the whole document, particularly the abstract, page 4 line 4 - page 8 line 3, page 22 line 16 - page 24 line 31). D9 is directed to bulk electrofusion.

D10 provides methods of fusing cells by chemical and electrical means (see the whole document, particularly the abstract, page 5 line 2 - page 8 line 5, page 15 line 3 - page 16 line 17, page 28 lines 7-24). D10 is directed to bulk electrofusion.

Electrofusion of individual single cell pairs is not new (see D11, and the references cited therein). The automated electrofusion of bulk cell populations is also not new (see D5, and the references cited therein). The teaching of D11 may be reliably combined with that of D5 to give the automated electrofusion of at least one desirous single cell pair, and therefore claims 1-4, 8-24, 27-43, and 45-47 are deprived of an inventive step when these two documents are combined.

None of documents D1-D10 disclose the individual positioning of single cell pairs prior to fusion, with the intention of generating desired fusates only. D2 and D3 teach that individual positioning of particles (two-celled embryos) reliably provides desired fusates. D2 or D3 may be reliably combined with D5 to give the automated electrofusion of at least one desirous pair of cells or embryos, and therefore claims 1-4, 8-24, 27-43, and 45-47 are deprived of an inventive step when these two documents are combined.

The use of a second pair of electrodes during cell electrofusion is also not new (see D7, and the references cited therein). The teaching of D11 may be reliably combined with that of D7 to give a method and apparatus for electrofusion of at least one single cell pair, and therefore claims 1-9, 14-19, 25-26, and 34 are deprived of an inventive step when these two documents are combined.

D4 provides methods of fusing cell populations by electrofusion (see the whole document, particularly column 7 line 49 - column 16 line 4, and claims 17-24), wherein cells are in contact with electrodes (see the abstract). Therefore D4 is not considered to deprive claims 1-71 of novelty or inventive step.

D8 provides methods and apparatus for electrofusion of cells (see the whole document, particularly the abstract, page 15 line 21 - page 16 line 14, example 1, and figures 1-5) wherein cells are in contact with electrodes (see Figure 4). Therefore D8 is not considered to deprive claims 1-71 of novelty or inventive step.

Supplemental Box II
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

Inventive step (IS) claims 1-43, 45-47 (continued)

Claims 44 and 51-57 meet the criteria set out in PCT Article 33(3) with regard to the requirement of Inventive Step because the prior art does not obviously suggest to a person skilled in the art the automated electrofusion apparatus having a second pair of electrodes, nor the pipette system of claims 51-57.

Industrial Applicability (IA) claims 1-71

Claims 1-71 appear to be industrially applicable.

THE CLAIMS:

1) A method of fusing first and second cells, the method including:
   a) Selecting at least one pair of a first and a second cell;
   b) Individually positioning each pair of cells such that the respective first and second cells of each cell pair are between two electrodes in a fluid filled fusing container, each cell pair being separated from each electrode and from each other cell pair; and,
   c) Applying a current having a predetermined waveform to the electrodes to generate a predetermined fusion pulse thereby causing the respective first and second cell of at least one pair of cells to fuse.
2) A method according to claim 1, the cells being held in suspension between the electrodes.
3) A method according to claim 1 or claim 2, the method including generating a DEP field, the DEP field being adapted to urge the cells towards each other.
4) A method according to claim 3, the predetermined waveform including a current representing the DEP field.
5) A method according to claim 3, the method including applying the DEP to a pair of second electrodes.
6) A method according to claim 5, the method including:
   a) Applying a DEP current to the pair of second electrodes;
   b) Positioning the first cell in the fusing container, the alternating field acting to attract the first cell towards one of the second pair of electrodes; and,
   c) Positioning the second cell in the fusing container, the alternating field acting to attract the second cell towards the first cell.
7) A method according to claim 6, at least one of the first and second cells being positioned in contact with at least one of the second pair of electrodes.
8) A method according to any one of the claims 1 to 7, the method including selecting the first and second cells using a pipette to extract:
   a) The first cell from a group of first cells held in a first container; and,
   b) The second cell from a group of second cells held in a second container.
9) A method according to claim 8, the method of positioning the first and second cells in the fusing container including:
   a) Using the pipette to position the first cell in the fusing container;
   b) Using the pipette to position the second cell in the fusing container, adjacent the first cell;

c) Positioning the electrodes such that the first and second cells are located substantially between the electrodes.

10) A method according to claim 8 or claim 9, the pipette being coupled to:

a) A drive system adapted to move the pipette with respect to the first, second and fusing containers; and,

b) An actuator adapted to actuate the pipette to thereby expel or draw in fluid through a port;

The method including using a controller coupled to the drive system and the actuator to move and actuate the pipette.

11) A method according to claim 10, the method of selecting a cell including causing the controller to:

a) Move the pipette such that the port is adjacent a cell having predetermined characteristics, the cell being held in fluid suspension in the respective container;

b) Actuate the pipette to draw in fluid through the port, thereby drawing in the cell and the surrounding fluid.

12) A method according to claim 10 or claim 11, the method of using the pipette to position the second cell adjacent the first cell including causing the controller to:

a) Move the pipette such that the port is adjacent the first cell in the fusing container;

b) Cause the pipette to expel fluid through the port, thereby expelling the second into the fluid in the fusing container;

c) Move the pipette such that the port is as close as possible to both the first and second cells;

d) Cause the pipette to draw in fluid through the port, thereby drawing in the first and second cells and the surrounding fluid;

e) Cause the pipette to expelling the first and second cells into the fluid in the fusing container; and,

f) Repeat steps (c) to (e) until the first and second cells are within a predetermined distance.

13) A method according to any of claims 1 to 12, the electrodes being coupled to an electrode drive system adapted to move the electrodes with respect to the fusing containers, the method including using a controller coupled to the electrode drive system to position the electrodes in the fusing chamber.

14) A method according to any one of claims 1 to 13, the electrodes being coupled to a signal generator, the method of applying the current to the electrodes including causing the signal generator to apply a predetermined current to the electrodes.

15) A method according to claim 14, the first and second cells having a respective cell type, the method including using a controller coupled to a signal generator to select the current in accordance with the cell types of the first and second cells.

16) A method according to claim 15, the first and second cells being the same type of cell and the first and second group of cells being the same group.

17) A method of fusing first and second cells, the method being substantially as hereinbefore described.

18) Apparatus for fusing first and second cells, the apparatus including:

a) A fluid filled fusing container;

b) At least two electrodes adapted to be positioned in the fusing container in use;

c) A selector for:

i) Selecting a first cell from a group of first cells held in a respective container; and,

ii) Selecting a second cell from a group of second cells held in a respective container;

iii) Individually positioning the respective first and second cells in the fusing container between the electrodes, so that the cell pair is separated from each electrode and each other pair of cells ; and,

d) A signal generator coupled to the electrodes, the signal generator being adapted to cause a field having a predetermined waveform to be generated between the electrodes, thereby causing the respective first and second cells of at least one pair of cells to fuse .

19) Apparatus according to claim 18, the selector being a pipette.

20) Apparatus according to claim 19, the apparatus further including:

a) A drive system adapted to move the pipette with respect to the first, second and fusing containers; and,

b) An actuator adapted to cause the pipette to expel or draw in fluid through a port.

21) Apparatus according to any one of claims 18 to 20, the electrodes being coupled to the fusing container.

22) Apparatus according to any one of claims 18 to 20, the apparatus further including an electrode drive system adapted to move the electrodes with respect to the fusing containers.

23) Apparatus according to any one of the claims 18 to 22, the current waveform including a fusion pulse, the signal generator being adapted to apply the fusion pulse to the electrodes to generate an electric field pulse thereby causing the cells to fuse.

24) Apparatus according to any one of the claims 18 to 23, the current waveform including a DEP current, the signal generator being adapted to apply the DEP current to the electrodes to generate a DEP field thereby urging the cells towards each other.

25) Apparatus according to any one of the claims 18 to 23, the apparatus including a pair of second electrodes, the pair of second electrodes being coupled to a second signal generator, the second signal generator being adapted to generate a DEP current, the DEP current being applied to the pair of second electrodes to generate a DEP field thereby urging the cells towards each other.

26) Apparatus according to claim 25, the pair of second electrodes being provided on the fusing container surface.

27) Apparatus according to claim 19 to 26, the apparatus further including a controller adapted to control the fusing of the cells by controlling operation of at least one of:

a) The pipette;

b) The electrodes; and,

c) The signal generator.

28) Apparatus according to claim 27, the controller including a processor coupled to at least one of:

a) The drive system and the actuator, the processor being adapted to move and actuate the pipette;

b) The electrode drive system, the processor being adapted to move the electrodes; and,

c) The signal generator, the processor being adapted to cause the signal generator to generate an electrical current having the predetermined waveform.

29) Apparatus according to claim 28, the controller including a detector adapted to detect the position of cells within the containers, the processor being responsive to the detector to move at least one of the electrodes and the pipette in response to the position of detected cells.

30) Apparatus according to claim 28 or claim 29, the processing system including an input for receiving input commands from a user.

31) Apparatus according to claim 30, the processor being coupled to a store for storing waveform data representing a number of different predetermined waveforms, the processor being adapted to select one of the number of predetermined waveforms in response to the input commands received from the user.

32) Apparatus according to claim 30 or claim 31, the processor being adapted to move at least one of the electrodes and the pipette in response to the input commands received from the user.

33) Apparatus according to any of claims 27 to 32, the controller being adapted to cause the cells to fuse by causing the apparatus to perform the method of any of claims 1 to 17.

34) Apparatus for fusing first and second cells, the apparatus being substantially as hereinbefore described.

35) A controller for controlling apparatus for fusing first and second cells, the apparatus including:

a) A fluid filled fusing container;

b) At least two electrodes;

c) A selector;

d) A signal generator coupled to the electrodes;

Wherein, in use, the controller is adapted to cause the cells to fuse by:

i) Causing the selector to:

(1) Select a first cell from a group of first cells held in a respective container; and,

(2) Select a second cell from a group of second cells held in a respective container; and,

(3) Individually position the respective first and second cells in the fusing container between the electrodes, the first and second cells being held in suspension, so that the cell pair is being separated from each electrode and each other pair of cells; and,

ii) Causing the signal generator apply a field having a predetermined waveform to the electrodes, thereby causing the respective first and second cells of at least one pair of cells to fuse.

36) A controller according to claim 35, the controller being further adapted to position the electrodes in the fusing container.

37) A controller according to claim 36, the controller including processor coupled to at least one of:

a) A drive system adapted to move a pipette with respect to the first, second and fusing containers;

b) An actuator adapted to cause a pipette to expel or draw in fluid through a port;

c) An electrode drive system adapted to move the electrodes with respect to the fusing containers; and,

d) The signal generator.

38) A controller according to claim 37, the controller including a detector adapted to detect the position of cells within the containers, the processor being responsive to the detector to move at least one of the electrodes and the pipette in response to the position of detected cells.

39) A controller according to claim 37 or claim 38, the controller including an input for receiving input commands from a user.

40) A controller according to claim 39, the processor being coupled to a store for storing waveform data representing a number of different predetermined waveforms, the processor being adapted to select one of the number of predetermined waveforms in response to the input commands received from the user.

41) A controller according to claim 35 or claim 40, the processor being adapted to move at least one of the electrodes and the pipette in response to the input commands received from the user.

42) A controller according to any one of the claims 35 to 41, the current waveform including a fusion pulse, the controller being adapted to cause the signal generator to apply the fusion pulse to the electrodes to generate an electric field pulse thereby causing the cells to fuse.

43) A controller according to any one of the claims 35 to 42, the current waveform including a DEP current, the controller being adapted to cause the signal generator to apply the DEP current to the electrodes to generate a DEP field thereby urging the cells towards each other.

44) A controller according to any one of the claims 35 to 42, the apparatus including a pair of second electrodes, the pair of second electrodes being coupled to a second signal

generator, the controller being adapted to cause the second signal generator to generate a DEP current, the DEP current being applied to the pair of second electrodes to generate a DEP field thereby urging the cells towards each other.

45) A controller according to any of claims 35 to 44, the controller being adapted for use with apparatus according to any one of the claims 18 to 34.

46) A controller according to claim 45, the controller being adapted to cause the apparatus to perform the method of any of claims 1 to 17.

47) A controller for controlling apparatus for fusing first and second cells, the controller being substantially as hereinbefore described.

48) A computer program product for controlling apparatus for fusing first and second cells, the computer program product including computer executable code which when executed by a suitable processing system causes the processing system to operate as the controller of any one of the claims 35 to 47.

49) A computer program product according to claim 48, the processing system being adapted to cause the apparatus to perform the method of any of claims 1 to 17.

50) A computer program product for controlling apparatus for fusing first and second cells, the computer program product including computer executable code which when executed by a suitable processing system causes the processing system to operate substantially as hereinbefore described.

51) A pipette system for manipulating particles, the pipette system including:

a) A nozzle for containing fluid in use, the nozzle including a port;

b) An actuator coupled to the nozzle, the actuator being adapted to draw in and/or expel fluid through the port; and,

c) An electrode coupled to the nozzle adjacent to the port, the electrode being adapted to cooperate with a second electrode to allow an electric field to be applied to coupled to one or more particles positioned adjacent to the port.

52) A pipette system according to claim 51, the electrode being formed a conductive tube.

53) A pipette system according to claim 52, the electrode being formed from a stainless steel tube having a diameter of approximately 10mm.

54) A pipette system according to any one of the claims 51 to 53, the pipette system including a drive system adapted to move the pipette system to be with respect to a fluid filled container to thereby allow particles to be positioned in or removed from fluid in the container.

55) A pipette system according to claim 54, the pipette system including a signal generator coupled to the electrode for generating a predetermined electric field between the electrode and a second electrode positioned in the container.

56) A pipette system according to claim 55, the pipette system including a controller adapted to control the drive system, the actuator and the signal generator to thereby apply an electric field to a particle by:

a) Positioning the particle in the container adjacent the second electrode using the pipette;

b) Positioning the pipette port adjacent the particle in the container; and,

c) Activating the signal generator.

57) A pipette system according to claim 56, the controller being adapted to fuse cells, by:

a) Positioning a first cell in the container adjacent the second electrode using the pipette;

b) Positioning a second cell in the container adjacent the first cell using the pipette;

c) Positioning the pipette port adjacent the first and second cells, such that first and second cells are substantially between the electrodes; and,

d) Activating the signal generator to cause a predetermined field sequence to be applied to the cells, thereby causing the cells to fuse.

58) A pipette system according to any one of the claims 51 to 57, the pipette system further including:

a) A radiation source; and,

b) A waveguide having a first end coupled to the radiation source and a second end coupled to the nozzle adjacent the port to thereby allow radiation from the radiation source to impinge on particles positioned adjacent to the port in use.

59) A pipette system according to claim 58, the pipette system including a detector, the detector being adapted to detect radiation emitted by the particle.

60) A pipette system according to claim 59, the detector being coupled to the first end of the waveguide, to thereby detect radiation emitted from the particle.

61) A pipette system according to any one of the claims 58 to 60, the radiation source being a laser.

62) A pipette system according to any one of the claims 58 to 61, the waveguide being a fibre optic cable.

63) A pipette system according to any one of the claims 58 to 62, the waveguide being formed from the nozzle, the nozzle including a shaped portion to allow the radiation from the radiation source to enter the nozzle and pass along at least a portion of the nozzle, the radiation being emitted from the nozzle through the port.

64) A pipette system according to any one of the claims 58 to 63, the pipette system including a controller adapted to perform at least one of:

a) Activating the actuator to thereby cause fluid to be drawn in and/or expelled through the port; and,

b) Activating the radiation source, to thereby expose a particle to radiation.

65) A pipette system according to claim 54 and claim 64, the drive system being coupled to a controller, the controller being adapted to recover particles having predetermined properties from the container by:

a) Positioning the pipette system such that the port is adjacent to a particle;

b) Activating the radiation source to thereby expose the particle to radiation;

c) Detect any radiation emitted by the particle;

d) Determine if the particle has the predetermined properties in accordance with the detected radiation; and,

e) In accordance with a successful comparison, activate the actuator to thereby draw fluid into the nozzle through the port, thereby recovering the particle.

66) A pipette system according to any one of the claims 51 to 63, the actuator including:

a) A fluid reservoir;

b) A flexible tube coupling the nozzle to the fluid reservoir;

c) An arm positioned so as to partially compress the tube;

d) An actuator drive system adapted to move the arm so as to perform at least one of:

i) Further compressing the tube to thereby expel fluid from the port; and,

ii) Decompressing the tube to thereby draw fluid in through the port.

67) A pipette system according to claim 66, the actuator drive system including:

a) A first actuator drive for moving the arm with respect to the tube and/or a bladder; and,

b) A second actuator drive formed from an arm end portion, the arm end portion being in contact with the tube in use, the second actuator drive being adapted to cause the arm end portion to expand or contract.

68) A pipette system according to claim 66 or claim 67, the pipette system including a controller coupled to the actuator drive system, the controller being adapted to operate the actuator drive system to thereby draw fluid in or expel fluid through the port.

69) A pipette system according to claim 68, the drive system being coupled to the controller, the controller being adapted to recover particles from the fluid by:

a) Positioning the pipette system such that the port is adjacent to a particle; and,

b) Activate the actuator drive system to thereby draw fluid into the nozzle through the port, thereby recovering the particle.

70) A pipette system according to any one of the claims 63 to 69, the tube being formed from silicon tubing.

71) A pipette system for manipulating particles, the pipette system being substantially as hereinbefore described with reference to the accompanying drawings.

DATED this 21st day of June, 2004

APPOLLO LEFE SCIENCES PTY LIMITED

By Their Patent Attorneys

DAVIES COLLISON CAVE